From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/036952	04.11.2004	07.11.2003

International Patent Classification (IPC) or both national classification and IPC
G01N33/50

Applicant
ACADIA PHARMACEUTICALS INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 3-87

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 3-87

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1,2

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	none
	No:	Claims	1,2
Inventive step (IS)	Yes:	Claims	none
	No:	Claims	1,2
Industrial applicability (IA)	Yes:	Claims	1,2
	No:	Claims	none

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

   and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

   see form 210

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

(see Item IV)

Re Item IV

Lack of unity of invention

1. The present application contains at least 6 inventions:

Invention 1: claims 1,2

The use of the FPRL1 receptor for identifying compounds effective in treating inflammation and associated pain.

Invention 2: claims 3,4 partially

The use of compounds "specifically active at the FPRL1 receptor" different from the compounds of formulae I, II or III for treating inflammation and associated pain.

Invention 3: claims 5,6 completely; claims 9-12 partially

Methods for screening agonists, antagonists, or compounds "able to affect one or more activities of a FPRL1 receptor"

Invention 4: claims 26-46 completely; claims 7-25 partially

Compounds of formula I and their use for treating inflammation and associated pain, other diseases and physiological states (as referred to in claims 8, 16-18, 20-24)

Invention 5: claims 47-59 completely; claims 7-25 partially

Compounds of formula II and their use for treating inflammation and associated pain, other diseases and physiological states (as referred to in claims 8, 16-18, 20-24)

Invention 6: claims 60-87 completely; claims 7-25 partially

Compounds of formula III and their use for treating inflammation and associated pain, other diseases and physiological states (as referred to in claims 8, 16-18, 20-24)

2. The reasoning is the following:

FPRL1 (formyl-peptide receptor like 1; see **D1**: Murphy et al., 1992) is also known as

lipoxin A4 receptor (LXA4R) (see D2: Deng et al., 1999;). FPRL1/LXA4R is notoriously involved in the inflammation process (see D3: Le et al., 2001, D4: Le et al., Trends in Immunology, 2002; D5: Cui et al., 2002; D6: Gewirtz et al., 2002; D7: Wang et al., 2001, etc.). Chemical compounds acting as ligands of FRPL1 are known (D8: Le et al., Int. Immunopharmacol., 2002). Methods have been set up to identify further agonists of FPRL1 (see D9: Klein et al., 1998). Uses of FPRL1 for identifying compounds effective in treating inflammation and associated pain do not necessarily depend upon methods for screening agaonists, antagonists or compounds "able to affect one or more activities of a FPRL1 receptor". The methods and uses of groups 1, 2 and 3 do not necessarily depend upon all compounds of groups 4, 5 or 6 and vice versa. The compounds, use of which is claimed in group 2, are structurally clearly distinct from either compounds of formulae I, II or III. Therefore, no special technical feature in the sense of Rule 13 PCT exists in between the identified groups of inventions.

3. Since no additional fees has been paid, the search has been limited to invention 1, *i.e.* claims 1 and 2. The present opinion is therefore restricted accordingly.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The present application relates to the use of the FPRL1 receptor as a tool to identify compounds effective in treating inflammation and associated pain.

2. The FPRL1 peptide is notoriously involved in inflammation processes and it has been suggested that FRPL1 would be a potential target for developing therapeutic agents (see for instance D7). Agonists of FPRL1 are known (see D8) and methods for identifying further compounds altering the activity of FPRL1 have been set up (see D9).

   In particular, D10 (WO0031261) explicitly discloses methods for identifying ligands, agonists and antagonists of FPRL1 that could act as potential drugs in inflammation processes and implicitly in the concomittent associated pain.

3. The subject-matter of **claims 1 and 2** is therefore neither novel or inventive and consequently does not meet the requirements of Art. 33(2) and (3) PCT.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO03106683	24/12/2003	12/06/2003	14/06/2002 15/07/2002
WO2004027427	01/04/2004	19/09/2003	19/09/2002
WO2005024057	17/03/2005	10/09/2003	10/09/2003